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The overarching goal of this project is to pursue a broad experimental program in futuristic research focusing on digital pathology and telepathology applications and practice, with the primary consideration being military medicine. The following areas are being addressed: 1) 2-D and 3-D digital image acquisition and virtual slide (VS) systems development for pathology applications; 2) Evaluation and testing of workstations and operating systems for digital pathology applications; 3) Testing and demonstration of ATM technology for digital pathology and telepathology purposes; 4) Evaluation, specification, and testing of an appropriate Object-Oriented Database Management System (OODBMS) for digital pathology purposes; 5) Evaluation, testing, and recommendation of a hierarchical storage management system (HSM) for digital pathology image recovery for local and telepathology referral basis; 6) Integration of National Library of Medicine (NLM) medical language resources (e.g. UMLS and SNOMED) to pathology image files for content-based retrieval; 7) Recommendations for FY 1996.

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"Development and Demonstration of a Networked Telepathology
3-D Imaging, Databasing, and Communication System: Phase I"

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INTRODUCTION

The overarching goal of this project is to pursue a broad experimental program in futuristic research focusing on digital pathology (DP) and telepathology (TP) applications and practice, with the primary consideration being military medicine. The specific needs of practicing Pathologists addressed in this effort are 1) Delays in delivery of samples and reports; 2) Reduction of time to examine a given number of images per patient; 3) Digital storage and retrieval of pathology imagery; 4) Availability of affordable high-quality imaging stations at primary and secondary sites; and 5) Availability of pathology reference images at primary and secondary sites.

The current research program has been carried forward to understand and address issues relating to a successful implementation and integration of future digital telepathology systems for Anatomic Pathology (AP) use in military medical settings, linking reference laboratories such as the Armed Forces Institute of Pathology (AFIP) to far-forward MASH facilities, ships, etc. This concept is depicted in Figures 1 and 2 below. All aspects of this
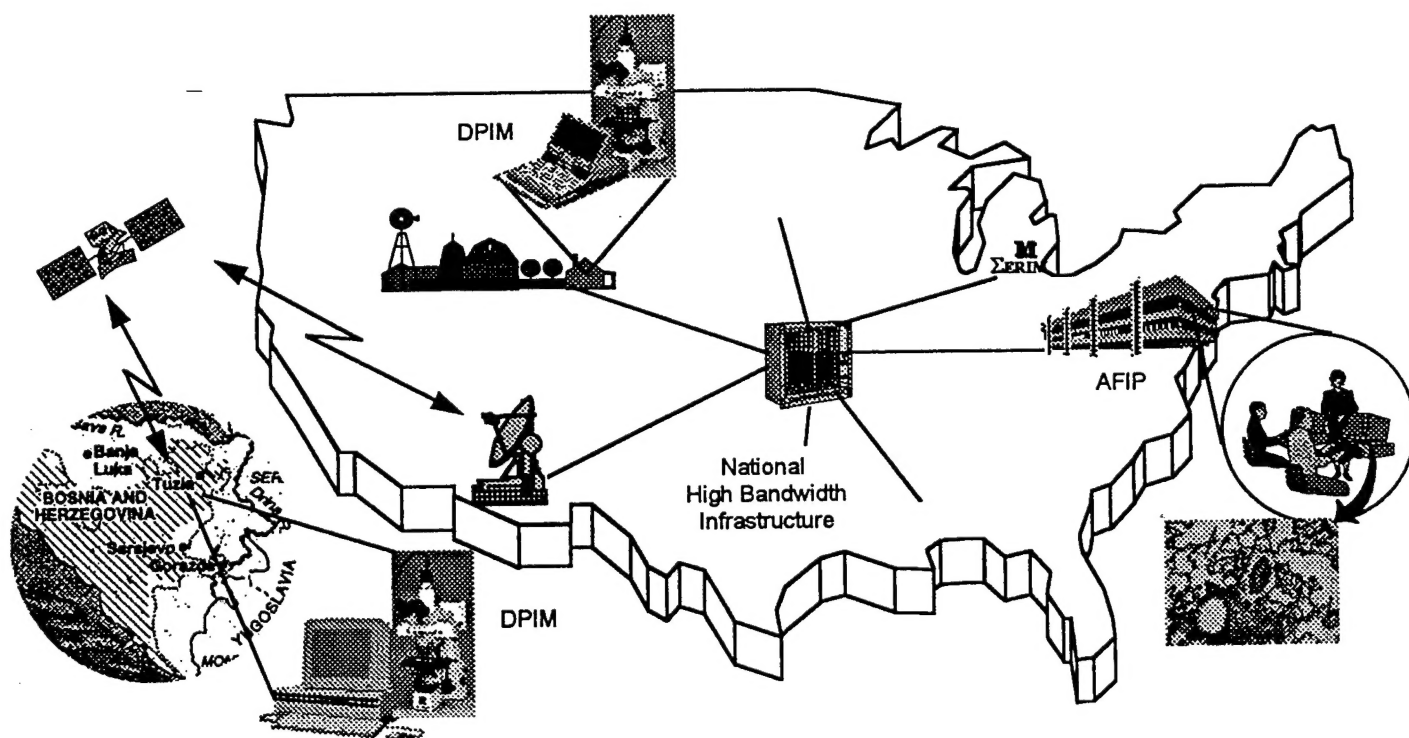

Figure 1: Vision of a fully deployed DP Imaging Microscope system for military medicine. Such an installation would enable the creation of a world-wide distributed DP laboratory (see Appendix V, for example). This report describes research to enable this vision.

problem have been examined in my digital microscopy imaging laboratory at the University of Michigan Medical School. There has been equal effort expended in examining software and integration issues as well as addressing hardware requirements and deficiencies. An

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underlying concern throughout this program relates not only to the high-speed transmission of pathology image objects for remote consultative diagnosis, but on how to organize these images and data objects for storage and retrieval when appropriate.

During this period, extensive consulting was done with members of the AFIP, with numerous visits made by all parties to both locations, UMich and AFIP. This was done to best insure that a product of most use to high-end military pathology application users would be produced. AFIP staff members consulted include Col. V. Ambrustmacher (Institute Director); Col. R. Becker (Quantitative Pathology); Maj W. Oliver (Forensics); Major A. El Sayeed (TelePathology); Dr. T. O'Leary (CytoPathology); and Dr. A. Noe (Medical Museum). Excellent team building was achieved during FY 1995, with the exception of Dr. El Sayeed, head of the AFIP telepathology program (See Appendix IV), who chose not to participate with the above group and the corporate partners (identified below). This proved to be a serious set-back to the other group members, as this project was perceived to be competition to this other effort. Dr. Athey (PI) also met with Dr. Hank Dardy of the Naval Research Laboratory (NRL) several times at the request of Dr. Satava at ARPA to obtain guidance and assistance on the deployment of ATM technology into and out of the AFIP to the University of Michigan Medical School.

The fields of DP and TP are very active at the present time (For reviews see Weinstein et al., 1989; Weinstein et al., 1995; Mun et al, 1995; Wray and Lai-Goldman, 1995; Richter et al., 1995; and Korpman, 1987). The field of "Pathology Informatics" has also emerged, and is an important area to study as it provides a natural context into which
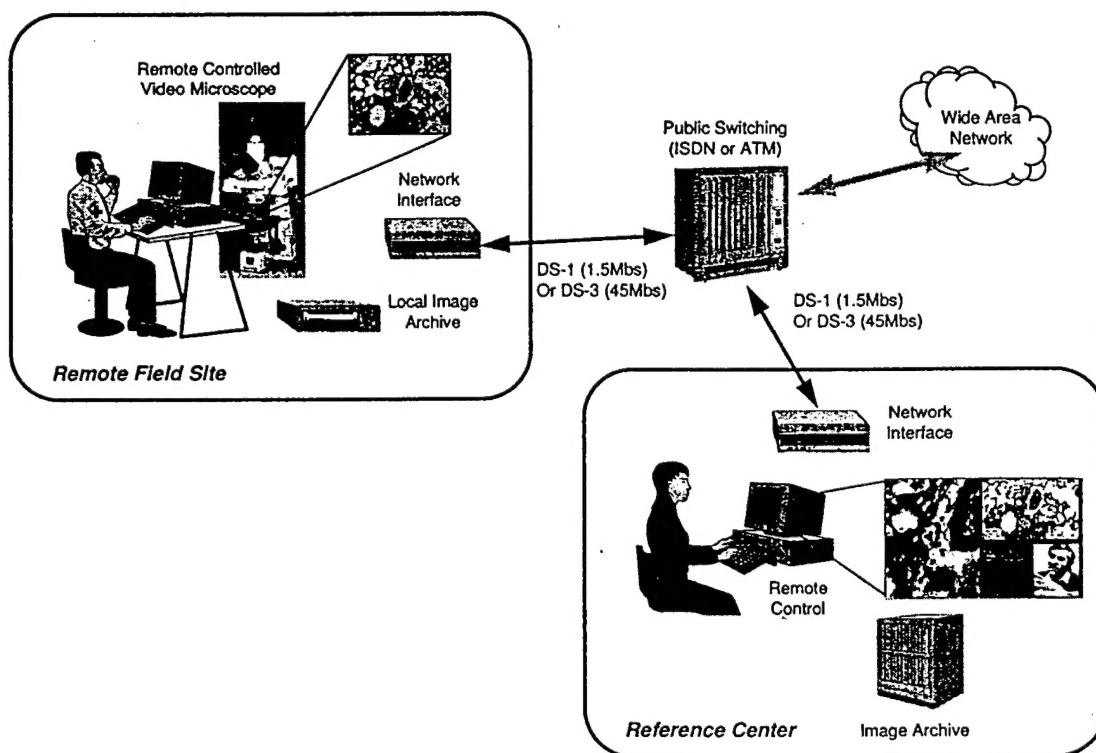

Figure 2: Research during this period focused on enabling functional links between remote field sites and the Pathology reference site(s) such as AFIP and my UMich laboratory.

DP imaging can be best understood by way of integration into the entirety of the DP medical record and archive, which includes information from the clinical laboratory information systems (LIS) side of pathology, which is classically housed in the "Clinical Pathology (CP)" area of the Pathology Department. This concept is discussed by Friedman (1990) and by Buffone and Beck (1993). In addition, several vendors have been offering video and digital TP imaging and data management systems that are designed to provide service to the remote field site. These include the SAMS automated microscope system (SAIC; San Diego, CA); the Apollo TP system (Apollo Software, Inc.; Alexandria, VA); IPI Samba (Imaging Products International; Herndon, VA); Roche Image Manager Research Triangle Park, NC); Image Path (Sony Medical Systems; Chicago, IL); and PATHNET (Cerner Corp., Kansas City, MO). Although these systems are taking their place in the civilian market place, I have chosen to focus on higher level research to enable a quantum leap in performance, scalability, and ultimately enabling a distributed DP worldwide network which allows for heterogeneous systems such as those above to interoperate. In this regard, I have discussed the ARPA funded telepathology project of Dr. Kendall Preston (Boeckler Instruments, Inc; Scottsdale, AZ) at length with ARPA Program manager Dr. R. Satava, and have agreed to focus my research on areas of DP and TP that would be most synergistic with the ARPA Advanced Biomedical Technology Program (ABTP).

After extensive discussions with ARPA, I have decided to pursue a strategy that will allow for the optimal interaction with industrial partners in this project. I have evaluated several partners and have chosen three: They are the Eastman Kodak Company (Rochester, NY), the Hewlett-Packard (H-P) Corporation (Federal Government Marketing; Washington, DC.), and Fore Systems (Pittsburgh, PA). Each have strong commitments to telemedicine, TP, and military medicine. One of the downsides of this strategy is that Kodak and H-P systems are currently not very well integrated. Officials from both companies, however, have assured me that these groups will participate fully to make our effort successful and sustainable.

The following areas are thus being addressed: 1) 2-D and 3-D digital image acquisition for pathology applications; 2) Evaluation and testing of workstations and operating systems for digital pathology applications; 3) Testing and demonstration of ATM technology for digital pathology and telepathology purposes; 4) Evaluation, specification, and testing of an appropriate Object-Oriented Database Management System (OODBMS) for digital pathology purposes; 5) Evaluation, testing, and recommendation of a hierarchical storage management system (HSM) for digital pathology image recovery for local and telepathology referral basis; 6) Integration of National Library of Medicine (NLM) medical language resources (e.g. UMLS and SNOMED) to pathology image files to enable content-based retrieval; 7) Commercial partnership considerations in digital pathology; and 8) Recommendations for FY 1996.

BODY

Methods

As an aid to evaluating progress, the following list is taken from page 7 of the grant proposal of Grant No. DAMD17-94-J-4512.

1. Link microscope and SGI Indy.
2. Enable multimedia capability on SGI Indy--Demonstrate conference ability to AFIP.

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3. Demonstrate voice to ASCII.
4. Integrate Kodak Photo CD writer.
5. Send micrographs and interactive overlay planes (arrows circles, etc.) to AFIP.
6. Strip headers, footers, and multimedia annotation to datafile for databasing.
7. Install object-oriented database on server.
8. Install Photo CD database software. Retrieve photos from thumbnails over the network from AFIP.
9. Install Ares Systems NLM UMLS and Medline search software.
10. Install RGB boards into Datacube system in DMSV and integrate 24-bit imaging into DMSV network.

The following format will be used in this section. Task worked on with goal, followed by methods used.

1) Evaluate and test workstations and operating systems for futuristic DP applications, including linking microscope to workstation. The following systems were evaluated: UNIX systems--Hewlett-Packard 9000 series, Sun Microsystems Solaris, and SGI Indy. Macintosh Power PCs were also evaluated. Evaluation criteria included the ability to acquire (e.g. Twain driver compatibility) and handle 24-bit color pathology imagery, interface with video and digital cameras, be compatible the chosen OODBMS, etc.

2) Test and demonstrate usefulness of ATM technology for digital pathology and telepathology purposes. Fore Systems ASX-200 series components were installed and their suitability for pathology image local area networks (LAN) and wide area networking (i.e. to AFIP using ARPA ATD test-bed) was evaluated. Test disk dumps, reads, writes, and image searches were made in my UMich facility moving several 1000 DP images from the image acquisition room(s) to other remote sites in other parts of the UMich facilities (which is several 1000 square feet, connecting many adjacent and non-adjacent rooms, some as many as 750 feet from on another.

3) Evaluate, specify, and test an appropriate object-oriented management system (OODBMS) for digital pathology purposes. Areas of evaluation included:

    *Heirarchal database design and implementation
    *Heirarchal image data management facility
    *Image coordinate capture for virtual slide (VS) application
    *Micrograph naming conventions
    *Object/feature naming conventions
    *Physical storage requirements
    *Automated data loading
    *Pathology data management facility
    *Interim and final evaluation results
    *Processing/sample handling history

4) Evaluate, test and recommend a hierarchical storage management system for digital pathology image recovery for local and TP referral basis. Careful performance measurements were made with the Kodak ADL-2000 system and the Unitree Data management system provided by H-P/Convex. System I/O, Disk read and write characteristics with error rate analysis, and the ability to batch digital pathology micrographs (upto 20MB an image, uncompressed) and associated text data were

examined. These data were compared to a similar data set that resided on a 2GB Hard disk.

5) <u>Integration of National Library of Medicine (NLM) medical language resources (e.g. UMLS and SNOMED) to pathology image files to enable content-based retrieval</u>.
This task was only started in Feb. 1995. Few careful tests have been made to date, although the basic system is installed and works on the H-P and Mac platforms.

Results

1) <u>Workstation</u>: Identification of H-P 770 series workstations for Reference TelePathology applications has been made. H-P will donate two of these to the program in FY96. H-P 715, 735, and 755 were evaluated and determined to have limited I/O capability for ATM applications. SGI Indy was not chosen as the corporation was not willing to partner with the consortium. The Power Macintosh was chosen as a back-up platform because of its compatibility with the Kodak DCS-420 digital camera system donated by Kodak. Both the H-P and the Macintosh systems were found to have the interactive multi-media capability needed for TP. The H-P systems were also found to have the server capability necessary to move the volume of imagery needed for pathology reference applications. Both the H-P and Mac systems installed have 24-bit data handling capability; thus the Datacube boards originally specified were not purchased and the DMSV Datacube system retired.

2) <u>Object-Oriented Database Management Systems (OODBMS) for Pathology</u>: The Versant object-oriented database management system has been chosen. This was tested by ERIM on a related contract, utilizing results obtained during Hoffmann-LaRoche production pathology imaging performed at UMich. Versant works well and is relatively easy to run and to use. Micrograph headers and other useful information such as operator, time, date, object examined, etc. were successfully stripped and placed into a test database system (FilePro, Microsoft Corporation; Seattle, WA). User generated interactive processing data was also loaded. Multimedia information has not been handled or integrated as yet.

3) <u>Pathology Image Analysis SW</u>: Work has been done with the Environmental Research Institute of Michigan (ERIM) to evaluate the NOESIS Vision Visilog development package for pathology-specific applications development. Visilog has 24-bit color processing capability and an easy-to-use Graphical User Interface. It will work on UNIX, DOS, and Mac platforms.

4) <u>Digital Camera</u>: Kodak contributed a 1000 x 1500 line 36-bit Color DCS420 to the program in FY95. Color calibration and increased frame acquisition speed is needed. This camera will work for remote applications where pathology still imagery is acceptable; however, further evaluation of suitable cameras is on-going. It is clear that a miniature 30 frame per second video camera for focusing will be needed, perhaps focusing through the eyepieces.

5) <u>3-D Microscope</u>: In FY95 a standard brightfield microscope was used in conjunction with the DCS-420 system, producing adequate color imagery for basic 2-D color histopathology diagnosis. A system with a moving stage will be identified and be procured that will also allow for the 3-D confocal images to be generated, as well as the new tasks of 2-D and 3-D "virtual slide" (VS) production (see below, also Appendix II).

6) <u>ATM Networking</u>: Fore systems ATM equipment was evaluated for use in pathology LANs and ATD purposes. The LAX-20 product did not provide consistent service to mux ethernet, FDDI, and ATM services, and cannot be used reliably as a router. The ASX-200 ATM switch has been tested. It was found to be reliable. It is proposed that a next generation ASX-200 product be procured in the beginning of FY 1997. One problem with ATM is the price for WAN service (see Appendix III) in and out of the Capitol region. Another problem has been that SAIC has not brought the ATM lines and the switch into the AFIP as promised. I spent a disproportionate amount of time trying to get this needed link enabled in time for the final system test in 1996.

7) <u>Voice recognition, Data Dictionary</u>: The National Library of Medicine (NLM) Unified Medical Language System word stock, semantic network, and relationships between terms was loaded onto an H-P 735 workstation. No voice recording system has been evaluated, purchased or integrated (yr. 2).

8) <u>Optical Storage Technology</u>: A 3/4 TB Kodak ADL 2000 near-line optical storage device was installed and tested using Unitree+ data management software on the H-P. This SW was unusable for pathology applications. The write rate is far below what is acceptable. Write rates were measured to be 110-160KB/s, with about 130KB/s being a typical write throughput rate. Given that the throughput was specified to be 1000KB/s, dividing by 2 since a read pass is needed to verify each write, and you get 500KB/s, nearly a factor of 4 greater than the measured performance. The reads, also, are about a factor of 4 slower than promised. The Kodak Multistore 3.0 Hierarchical Data Management system will be implemented FY 1996 as a replacement. This will give the best available storage solution for the images generated during the remainder of the program, and the best follow-on potential for future work with NRL.

Kodak optical photo CD technology was evaluated for integration into the microscope workstation. Several reasons are given to hold off until FY 1996 for further action. They are: Unavailability of 8x-speed worm drives with SW for this product. Research indicates that 16x drives form Phillips and others will be available. Also, the Kodak software for photo-CDs only runs on Macintosh and Sun workstations, but in SunView (an older Sun operating system). This has made it impossible to use this software to send thumbnails back and forth to AFIP. No one supports this OS any longer, and meetings with Kodak managers in Rochester, NY gave me no confidence that photo CDs will be a major player in the years to come, partially owing to the proprietary data compression technology

<u>Scaleable Compute Technology</u>: The H-P 770 workstation was chosen to be compatible with the H-P/Convex scaleable platform, which is being tested in a companion project.

CONCLUSIONS

Progress has been substantial and project delivery is on time (see appendix I). I have had significant interaction and direction from the sponsor (ARPA) who have visited my facilities several times to see the progress. During one of these visits, I proposed to add a task to the statement of work to make this project more relevant to the practice of pathology. (I am a microscope imaging specialist who is learning about the pathology application by doing it!) The following is a synopsis of the state of the art for telepathology (TP) imaging systems and is a redirection of the project to meet the aim of a futuristic and usable integrated TP devices. This redirection came as a result of correspondence with Dr. R. Becker of the AFIP whose nomenclature and description I use liberally below.

The core of telepathology is transmission of microscopy images and their interpretation by a remote consulting pathologist. The large amount of image data available from histologic slides, coupled with the requirement that pathologists wish to review the entire slide, makes TP an even more challenging application than teleradiology. TP developers have focused on two technical strategies. The more robust is robotic video microscopy (RVM), in which the consulting pathologist views images that are acquired and transmitted in real time during remote manipulation of an automated microscope. A major strength of this approach is that the pathologist can examine images from almost any area and focal plane that would be accessible "hands-on" at the examination microscope. The main limitations have been assured and affordable access to bandwidth for real-time transmission of high resolution images, tradeoffs between field of view and resolution of displayed images (see Figure 3), the relatively slow response in remote manipulation of the microscope and slide (especially if satellite transmission must be used), and the analog nature of video imaging.
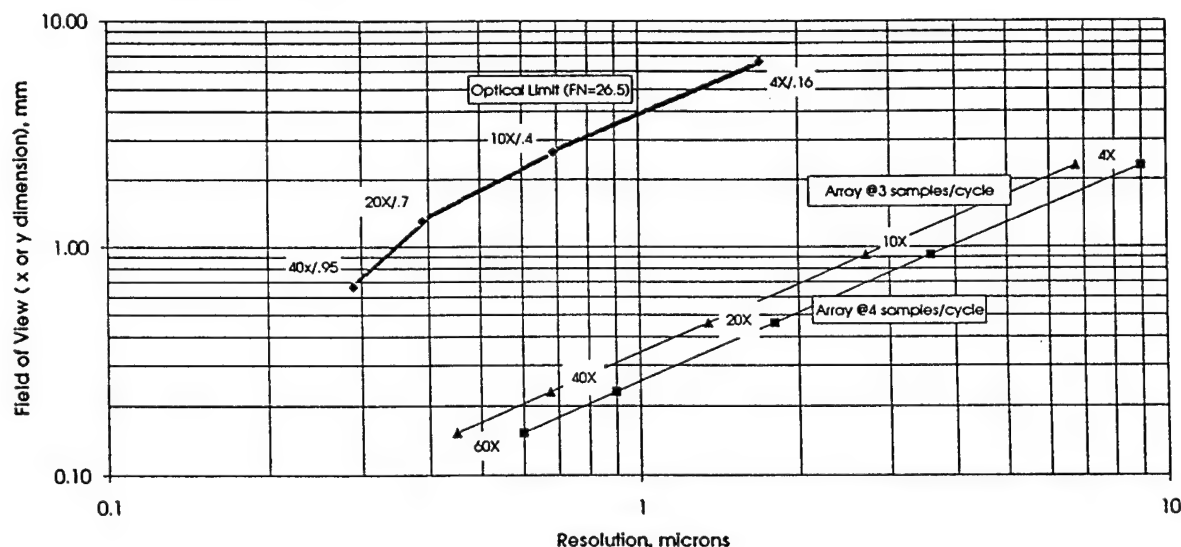
Figure 3: Field of View vs. Resolution (1024x1024 Array, 9 micron pitch) Compared with Optical Limit

A simpler TP approach is selective video microscopy (SVM), in which digitized image frames are obtained for diagnostic interpretation at one site, and transmitted for diagnostic interpretation at another. SVM's main advantage is much lower cost for equipment to acquire, send and display images. Once acquired, the images are sent automatically and stored for the receiving pathologist to review at will (with optional interactive consultation via voice hookup and perhaps matched image overlay generation). The selective aspect of image acquisition raises serious issues for SVM use in consultation. SVM forgoes the important low magnification information that a consulting pathologist would use before changing to high magnification. Almost always, the transmitted images represent a small part of the specimen on a slide, counter to the usual standard of care. Of greatest concern is the possibility that poorly selected image frames will convey an inaccurate impression of the slide as a whole or will omit diagnostic areas that would have been important to a consultant working with the actual slide. This concern is reinforced by the circumstance that the individual selecting images from diagnostically difficult cases presumably does not know "the answer" and so has an incomplete idea of just what areas to digitize.

One or two other TP designs are meant to provide many benefits of both RVM and SVM while mitigating the drawbacks of either. They provide remote microscope control and real time transmission of low resolution images for field selection, then acquisition and transmission of high resolution image frames for final interpretation. Overall, however, the tradeoffs made in all designs so far yield systems that lack the ease of use and completeness of information transfer associated with hands-on microscopy. We have decided (with the strong encouragement of Col. R. Becker, MC, of the AFIP). To develop a virtual slide (VS) application which would essentially capture the entire histological specimen image present on the tissue specimen.

A complete VS application will provide real time access to previously transmitted images representing all areas of the slide, at display resolution matching that of the microscope optics. VS depends on intensive use of available technologies for image acquisition, compression, transmission, storage, and recall/display to allow optimal diagnosis. Though the microscope must be automated, its remote control is not an issue with VS. Data acquisition is an important but relatively straightforward problem to solve. Data volumes on the order of 250 Gbytes (uncompressed) per slide are possible, though most volumes will be in the 2 GB range. It is likely that the most challenging problem will be recall and display of the transmitted images with speed and flexibility comparable to that enjoyed in direct microscopy.

The features to balance are resolution of the displayed images, size of the field of view, image update rate, and ease of using the interface to specify an xyz location for display. Much of the challenge for recall/display technology is in fulfilling update requests that rapidly and arbitrarily skip about the data volume. It is possible that dynamic refinement of images will ease some of that demand, depending on correlation with studies of human visual perception.

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9/26/95

Progress Report for BAA 94-14

"Development and Demonstration of a Networked Telepatholgy 3-D Imaging, Databasing, and Communications System: Phase I

Progress was made on all aspects of BAA 94-14 in FY 1995. These include workstation choice and procurement, digital camera procurement and evaluation, pathology-specific software and database evaluation, optical archiving technology, and ATM networking. Specific recommendations for FY 1996 have been made to Drs. Satava, Jenkins, and Jones to expand the scope of the program and provide successful delivery of technology and ATD with NRL and AFIP.

Workstation:	Identification of HP 770 series workstation as preferred workstation for reference telepathology applications. H-P will donate two workstations to project one to ERIM for development and one to AFIP for testing in the beginning of FY 1996. H-P 715, 735, and 755 were evaluated and determined to have limited I/O capability for ATM applications.
Database:	Versant object-oriented database has been chosen. This has been tested in the Hoffman-La Roche production pathology environment of the University of Michigan. It works well and is flexible and easy to use.
Pathology Image Analysis SW:	Work has been done with ERIM to produce pathology specific software using NOESIS Vision's Visilog development package. EAI and Inovision, Inc. software have not been used, owing to lack of features for pathology applications. Visilog has full color processing capability and an easy-to-use-and-develop Graphical User Interface.
Kodak Optical Technology:	Kodak ADL 2000 system was installed and tested using Unitree+ Data management software. Dsicussions with Kodak are ongoing to provide for testing of Multistore 3.0 hierarchical storage manager. In addition, Photo CD/H-P integration is being pursued.
Digital Camera:	Kodak contributed a 1000x1500 36-bit DCS420. Color

calibration and increase frame speed is needed. This camera will work for remote applications, however. Further evaluation of suitable cameras is ongoing.

3-D Microscope:

This year we have been using a standard laboratory brightfield microscope. I have evaluated the Meridican ACAS Ultima 570 for FY 1996 procurement.

ATM Networking:

Fore Systems ATM equipment has been evaluated for use for the pathology environment and ATD purposes. The LAX-20 product did not provide consistent service to mux as ethernet, FDDI, and ATM services and cannot be used reliably as a router. A Cisco product is under evaluation. The ASX 200 ATM switch has been tested reliably and is recommended for deployment at AFIP.

Scalable Compute Technology:

HP 770 was chosen to be compatible with Convex platform, which was tested in another project.

Data Dictionary and Voice Recognition:

It is suggested that the Keurzeweil-specific pathology product be evaluated in FY 1996. The NLM compatible meta-language dictionary that will be used will be provided by Dr. Paul Clayton of Columbia University School of Medicine (in negotiation)

Brian:

To my great annoyance, I've lost my original write-up of times and costs for transmitting a "virtual slide." I've rerun the calculations below from scratch, but with assumption of a larger specimen area for each slide. Another important change is that I've doubled the dollar costs from what I mentioned to you, to reflect fact that carrier charges (see chart on page from Network World) apply **both** to sender and receiver.

The calculations below are for very demanding circumstances. These include: a) digitization of entire 40 mm by 22 mm coverslip area at 5 z-levels, with xy sampling frequency (0.25μ spacing for square, 100% fill pixels) between one and two times the nominally resolved frequency of the optical system, b) 24 bit deep pixels, c) no compression, d) 10% oversampling needed in x and y for image registration, e) 10% transmission bandwidth loss for packetting and resends. Data sampling frequency is always a touchy topic. We should discuss the relevant numbers further before going out to anyone with this idea.

An "optimistic" factor I've used is assumption that 100% of the carrier-provided bandwidth will be used, i.e. we completely fill a constant bit rate (CBR) line 24 hours a day every day. This assumption does not affect calculations of data volume or specimen transmission time, but does affect the ultimate cost per specimen estimate since carrier's CBR charges accrue whether or not data are in the pipe. Different models for line use might be more appropriate, but not as easy to calculate below.

I. Data volume calculation:

$$\frac{5 \text{ Level}}{\text{CovSlip}} \times \frac{40\text{mm} \times 22\text{mm}}{1 \text{ Level}} \times \frac{1E6 \ \mu^2}{1 \ \text{mm}^2} \times \frac{1 \text{ Pixel}}{.0625 \ \mu^2} \times \frac{1.21 \text{ CovSlip}}{\text{DataSet}} \times \frac{3 \text{ Byte}}{1 \text{ Pixel}} \times \frac{1 \text{ GByte Data}}{1E9 \text{ Byte}} = \frac{255.5 \text{ GByte Data}}{\text{DataSet}}$$

II. Transmission rate calculation:

DS3 CBR Line

$$\frac{1\ sec}{45\ Mbit} \times \frac{8E3\ Mbit}{1\ GByte} \times \frac{1.1\ GByte}{1\ GByte\ Data} \times \frac{1\ hr}{3600\ sec} = \frac{.05432\ hr}{GByte\ Data}$$

OC3 CBR Line

$$\frac{1\ sec}{155\ Mbit} \times \frac{8E3\ Mbit}{1\ GByte} \times \frac{1.1\ GByte}{1\ GByte\ Data} \times \frac{1\ hr}{3600\ sec} = \frac{.01577\ hr}{GByte\ Data}$$

III. Transmission cost/hr (fixed cost, excludes startup):

DS3 CBR Line

$$\frac{1\ Month}{730\ hr} \times \frac{\$4220}{Site\text{-}Month} \times 2\ Sites = \frac{\$11.56}{hr}$$

OC3 CBR Line

$$\frac{1\ Month}{730\ hr} \times \frac{\$8300}{Site\text{-}Month} \times 2\ Sites = \frac{\$22.74}{hr}$$

IV. Transmission time/slide (from I and II above):

DS3 CBR Line

$\dfrac{255.5 \text{ GByte Data}}{\text{DataSet}} \times \dfrac{.05432 \text{ hr}}{\text{GByte Data}} = \dfrac{13.87 \text{ hr}}{\text{DataSet}}$

OC3 CBR Line

$\dfrac{255.5 \text{ GByte Data}}{\text{DataSet}} \times \dfrac{.01577 \text{ hr}}{\text{GByte Data}} = \dfrac{4.03 \text{ hr}}{\text{DataSet}}$

V. Transmission cost/slide (from I - III above):

DS3 CBR Line

$\dfrac{255.5 \text{ GByte Data}}{\text{DataSet}} \times \dfrac{.05432 \text{ hr}}{\text{GByte Data}} \times \dfrac{\$11.56}{\text{hr}} = \dfrac{\$160.43}{\text{DataSet}}$

OC3 CBR Line

$\dfrac{255.5 \text{ GByte Data}}{\text{DataSet}} \times \dfrac{.01577 \text{ hr}}{\text{GByte Data}} \times \dfrac{\$22.74}{\text{hr}} = \dfrac{\$91.62}{\text{DataSet}}$

Certain factors would probably allow lower cost per slide by decreasing the size of the dataset. One is use of image compression, for which Bill and I estimate a 50% reduction in transmitted bytes. A second is the more realistic and testable assumption that, on average, tissue from a single block cut occupies only about one-quarter of the coverslip area on a slide. Other "savings" might be practical, but applying only compression and smaller sample area decreases estimate of per-dataset resources used by compression and smaller sample area decreases estimate of per-dataset resources used by 1.73 hr and $20.05 for DS3 or .50 hr and $11.45 for OC3.

My conclusion is that time and dollar cost for transmission alone do not rule out the "virtual slide" application linking centers that can justify line costs overall. The images have to be greater challenges are probably in image acquisition and display. The images have to be digitized from autofocused views, corrected for lighting variation, and frame-by-frame

registered at subpixel precision prior to compression and transmission. These are heavy duty tasks, but should be fully automatable. For replay (either before or after transmission), data must be displayable at rates mimicking use of a standard light microscope (including z-plane movement). Display of resampled data (presenting lower power views) and frame-registered switching between magnifications must be supported. I believe these features are a greater technical challenge than digitization, since we'll need essentially arbitrary subframe-wise retrieval and display at 60 Hz, driven by user commands through something like a mouse/joystick interface. **My question to you is whether such access/display rates are now practicable by Hewlett-Packard or another consortium member.** If so, I think development of a virtual slide application would be a very competitive proposal for telemedicine funding. The value of such an application in relieving static telepathology's field sampling problem is clear. Bandwidth demand might be less than for dynamic telepathology using similar resolution. Other applications in scale-dependent quantitative image analysis also come to mind.

REPRINTED FROM ——

Bell Atlantic unveils flexible ATM pricing

RBHC files nation's first ATM tariff with FCC.

BY DAVID RHODE

Washington, D.C.

Claiming pent-up ATM demand from about a dozen federal agencies, Bell Atlantic Corp. last week filed the nation's first Asynchronous Transfer Mode tariff with the Federal Communications Commission.

Under the filing, government users have great flexibility in choosing the speed of the ATM service they need and can specify whether their applications will consist principally of variable bit rate (VBR) or constant bit rate (CBR) traffic.

Users that can accept the less deterministic VBR option will enjoy a price schedule that saves them 5% to 10% compared to CBR switching, which is generally required for voice and high-resolution video.

"It's a way to give a little bit of a price break to the data user," explained Geri Cerkovnik, a Bell Atlantic program manager.

Bell Atlantic's offering — which is limited to federal agencies in the Washington, D.C. region — appears likely to contribute to the armed forces' accelerating movement toward ATM transport in metropolitan- and, potentially, wide-area networks (*NW*, July 25, page 1).

Among the users that had been waiting for the carrier's filing is the Walter Reed Army Medical Center. The military's flagship hospital in the nation's capital has contracted for a network that requires medical images to be sent over the local and metropolitan areas in two seconds or less, said Lt. Col. Gary Gilbert, the hospital's director of information management.

Most of that time is required for archive retrieval, leaving less than one second for a 2M- to 4M-byte medical image to be transmitted, Gilbert said. Only ATM provides the bandwidth and the flexibility to provide this speed consistently, he said.

In consultations with Bell Atlantic officials before the tariff filing, Walter Reed officials stressed the need for flexible bandwidth requirements, Gilbert noted.

The tariff allows users to choose bandwidths from 1.5M to 155M bit/sec in increments as small as 500K bit/sec, although the access link to Bell Atlantic must be at least 45M bit/sec (see graphic).

If the user selects prices off the CBR schedule, the designated bandwidth is a "peak cell rate," or maximum throughput, explained Curt Koeppen, director of federal military programs for Bell Atlantic.

If the user selects prices off the VBR schedule, the designated bandwidth is a "sustained cell rate," or average throughput, above which the user can burst for a nominal additional fee, he said.

The carrier filed a formal tariff rather than issue price sheets or specify rate ranges like some others (*NW*, July 18, page 1) because of government procedures, Cerkovnik said. "Predictability of pricing is a very important item because they're budget-constrained," she said.

The tariff does allow the government to authorize additional users under the price schedules.

In practice, that means interexchange carriers may be given the opportunity to buy off the schedule to connect government ATM users in Washington with those outside the local access and transport area, Koeppen said.

And the pricing scheme could serve as a model for a general rollout of ATM service by Bell Atlantic, Koeppen said.

"The Bell Atlantic commercial side of the world will be filing [an ATM tariff] in 1995," he added.

To support the ATM offering, the regional Bell holding company has installed two AT&T GCNS ATM carrier switches connected by a Synchronous Optical Network backbone, Koeppen said. ∎

Bell Atlantic's scalable ATM pricing	
45M bit/sec access	
First 1.5M bit/sec	$2,000
Each additional 0.5M bit/sec	$60
Up to a maximum	$4,220
155M bit/sec access	
First 10M bit/sec	$4,100
Each additional 1M bit/sec	$70
Up to a maximum	$8,800
Variable bit rate (VBR) switched service prices/month	
45M bit/sec access	
First 1.5M bit/sec	$1,900
Each additional 0.5M bit/sec	$50
Up to a maximum	$3,750
155M bit/sec access	
First 10M bit/sec	$4,000
Each additional 1M bit/sec	$60
Up to a maximum	$7,600

Designated speeds under CBR service are peak cell rates, or maximum possible throughput. VBR figures are sustained cell rates, or average throughput; users can burst above designated rate for a nominal additional fee.
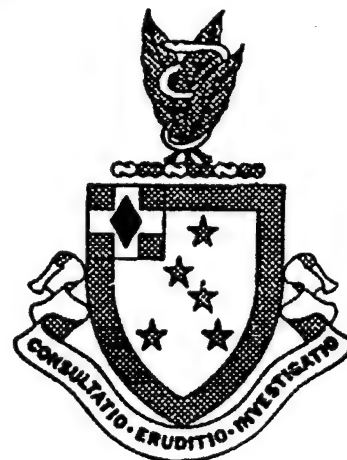
The TelePathology Project

The Armed Forces Institute of Pathology (AFIP) has a rich history in U.S. military medicine, tracing its beginnings to the Army Medical Museum in 1862. Today this tri-service agency and world leader in pathology responds annually to over 45,000 surgical pathology and autopsy consultation cases for diagnosis and quality assurance from around the world, including the investigations of military and civilian aircraft accidents.

Each year the Institute offers over 50 postgraduate medical education courses for civilians as well as the military and conducts advanced research techniques to study disease processes, including electron microscopy, digital image processing, and DNA probes. AFIP's diagnostic expertise, international tissue repository with over 2 million cases and 55 million pathology slides, ongoing research programs, and specialty education programs combine to make it a world resource in pathology excellence and a major element in assuring quality of patient care.

Since March 1993, the AFIP has been providing Telepathology service in the form of diagnostic consultations to remotely located Army, Navy, Air Force and civilian pathology laboratories. The AFIP will shortly extend the same service to several other civilian and Veteran Administration Medical Centers. In addition to using systems utilizing wide band width communication links, the AFIP's Telepathology Service can use conventional telephone lines to receive cases from referring laboratories. Using such a simple affordable link, cases were sent from Europe to the AFIP on an experimental basis. Planning is underway to link six Foreign Telepathology Centers in Great Britain, France, Germany, Switzerland, Sweden and Norway to the AFIP on permanent basis.

As the 21st century approaches, the AFIP continues its vital role in military and civilian medicine.

The Telepathology Project

At The Armed Forces Institute of Pathology

Why does the AFIP pursue Telepathology?

The AFIP's mission dictates a continuous endeavor to improve its consultation service. This encompasses making its service more available and more timely, thus bringing the skill of its experts to bear with beneficial impact on direct patient care.

What is wrong with the current mail-in consultation pathway?

Nothing is fundamentally wrong with the mail-in. However, we believe that in a good proportion of cases we may be able to help the contributor in a matter of hours rather than days. This can translate to peace of mind for the pathologist, the clinical team and most importantly the patient. Also it can help retain pathologists in rural areas, solo practices and remote military sites where overnight mailing may not be an option. The mail-in will always be the fall-back when a case can not be resolved by means of telepathology.

What is the cost for activating a site and per case cost?

A site can be activated for less than $15,000. This includes a standard resolution unit with deployment and training. Communication costs are that of a 6 to 10 minutes (for 12 to 20 images) long distance phone call and the cost of health professionals' time on both ends. You can make your dollar go far if you request an answer in a matter of hours rather than real time.

Telepathology

Telepathology is the practice of Pathology at a distant location utilizing means of telecommunication.

The Armed Forces Institute of Pathology has an active telepathology program. The project was initiated in 1991 and it entered active service in March 1993 by providing patient centered diagnostic pathology service to three remote military hospitals.

In its first eight months of operation it received over 180 telepathology cases for consultation. The cases are enrolled in a pilot study that compares telepathology to conventional mail-in consultation in terms of diagnostic accuracy, impact on patient care and cost of consultation.

The program held its First International Seminar and Workshop on Telemedicine in May 1993, with faculty from six European countries, eight national institutions, the AFIP and participation of five major corporations.

For further information contact:

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The Test Sites

Moncrief Army Community Hospital
Fort Jackson, South Carolina
140 Beds; 2 Pathologists; 5,100 Surgicals; 5,500 Cytologies; 12 Autopsies

Millington Naval Air Station Hospital
Millington, Tennessee
100 Beds; 1 Pathologists; 3,400 Surgicals; 5,000 Cytologies; 1 Autopsy

Wright Patterson Air Force Base Hospital
Dayton, Ohio
275 Beds; 6 Pathologists; 13,000 Surgicals; 43,000 Cytologies, 30 Autopsies
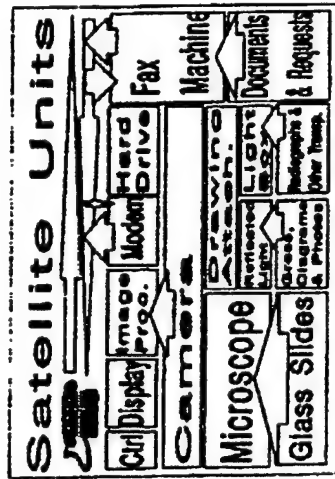
Satellite Units

Diagram of
Integrated deployable Field Unit, Generation I (IDFU-I)

- Low-cost, hospital-wide, mobile, takes minutes to setup
- Structured on-site training, given by 6 man-day effort
- Uses conventional telephone lines, connect time 30sec/image

The Pilot Study

To assess telepathology consultation needs and case composition we equipped three hospitals (Navy, Army and Air Force) staffed with one, two and multiple pathologists respectively by IDFU-I. For each consultation case the pathologist initiates a telepathology mail-in and a telepathology consult simultaneously. AFIP issues a report after examining the images and an independent additional report after examining the pathology slides received by mail.

Preliminary Findings:

. The images enabled accurate diagnosis

. The system encouraged consults

. The solo practitioner used it more

AFIP Telepathology Program
Publications in 1993

OBSERVER'S ANALYSIS OF LIGHT MICROSCOPY IMAGES IN THE FIELD OF ANATOMIC PATHOLOGY

A. K. Bleyard, M.D., Norman J. Carr, MRCPath, and James H. Scales, M.D., from Armed Forces Institute of Pathology, Washington, D.C., the Uniformed and Naval Air Force Institute of Pathology and Tropical Medicine, Dallas, TX.

In the field of anatomic pathology the pathologist utilizes a variety of data to produce a diagnosis. Of paramount importance is the visual image as seen through a light microscope. We have attempted to describe this image in both quantitative and qualitative terms. A comprehensive understanding of the inherent characteristics of this image is mandatory if a new medium, such as Telemedicine, is to be introduced into the conventional specimen-microscope-pathologist continuum.

The microscopic field of a compound microscope is a circular virtual image appearing to be to be 8cm in diameter and projected 10cm from the observer. This results in a magnified field of view measuring 44 degrees in visual arc. The number of picture elements (pixels) resolvable by the human eye in this virtual image [a limited primarily by the acuity spectrum (Hz) of the observer. For a typical 1Hz spectral visual acuity of the objective and secondarily by the with Hz=0.30, approximately 1700 pixels are resolvable. The number of simultaneously viewable colors is determined by both the intensity of light used and the eye's ability for color separation in the blue, red and green color bands.

PREPROPOSAL

Title: Remote Automated Digital Imaging Microscopy for
           Cervical Cytologic Diagnosis (The Distributed Cytology
           Laboratory)

Principle Investigator: Timothy J. O'Leary, M.D., Ph.D.
                                 Department of Cellular Pathology
                                 Armed Forces Institute of Pathology

Associate Investigators: Brian Athey, Ph.D.
                                 Department of Pathology
                                 University of Michigan

                                 Robert L. Becker, Col., MC, USAF
                                 Department of Cellular Pathology
                                 Armed Forces Institute of Pathology

OBJECTIVE: To increase the speed and accuracy of cervical
               cytologic diagnosis by implementation of automated
               prescreening strategies and use of remote digital
               microscopy.

Introduction

Examination of cervical cytologic specimens (Pap smears) is
the most common anatomical examination carried out in the
laboratory; two to four million such examinations are
conducted yearly on military personnel or their beneficiaries.
Unlike examination of other cytologic or biopsy material,
initial examination of the Pap smear is conducted by a trained
cytotechnologist. The cytotechnologist is expected to screen
50 to 100 slides daily, and to reliably detect a few abnormal
cells which may be expected in approximately 3 to 5 percent of
cases. The result is generally satisfactory, but
approximately 5% of cases with abnormal cells present on the
slide are missed in even the best of laboratories.

Various approaches to the examination of Pap smears are
employed in various institutions. Large hospital laboratories
typically have a staff of several cytotechnologists who
perform examinations under the supervision of a
subspecialty-certifed cytopathologist. These laboratories
typically have a sufficient staff to insure good turnaround
times under most circumstances. In addition, the presence of
the highly trained cytopathologist assures accurate diagnosis
of even the most difficult cases.

Smaller installations may rely upon the services of a general
pathologist examining smears with or without assistance from a
cytotechnologist, cytology service contracts with local

laboratories, submission (by mail) of specimens to a few large screening centers (as implemented by the Air Force). Within the Department of Defense, all these strategies are currently employed, and difficulties are encountered with each approach. For example, the Naval Medical Clinic of New Orleans received cytology support from an independent laboratory which lost its federal license following an investigation and broadcast by a major national television network. Wilford Hall USAF Medical Center was forced to send slides sent to its Air Force Cytocenter to a second cytocenter when a cytotechnologist shortage occurred; this was possible only because the second center had maintained excess capacity, which is in itself wasteful.

Remote digital microscopy may provide a mechanism by which to design a "virtual laboratory" in which cytotechnologists and pathologists can carry out their functions though physically located thousands of miles from each other and from the patient. Slides may be stained and digitized in the clinic, and, after electronic imaging, examined by cytotechnologists throughout the country or the world. Pathologist review of abnormal specimens may similarly be distributed; consultation among pathologists regarding difficult cases will be facilitated. In this document, the concept of the Distributed Cytopathology Laboratory (DICL) will be presented, together with a proposal for a feasibility demonstration.

The Distributed Cytopathology Laboratory (DICL):

The steps in obtaining, examining and reporting a Pap smear are as follows:

1. The smear is obtained by brushing a woman's cervix during a clinic-based gynecologic examination. The brush is smeared on one or two microscope slides, and the slides are fixed immediately by immersion in ethanol or by spraying with an aerosol spray fixative.

2. The slides, together with an accompanying SF541, are transported to the clinic laboratory. If examination is to take place elsewhere, the slides are packaged and mailed. Depending on case volume, slides may be retained for several days prior to mailing while cases are collected.

3. After receipt in the examining laboratory, slides are inspected for breakage in the mail, and demographic/clinical information from the SF541 is entered in the laboratory computer system. Slides are stained, either manually or with an automated staining system. Slides are then examined by a cytotechnologist. Reports on slides without

abnormality are rendered by the cytopathologist. Slides with abnormalities are referred to a senior cytotechnologist and/or a pathologist for further examination and final reporting, following identification of abnormal fields by the use of ink dots applied to the slide.

4. The final diagnosis is recorded on the computer system. Reports are mailed, sent by facsimile transmission, or reported over a computer network.

If the examining laboratory is not collocated with the clinic, this process may take several weeks. Similar turnaround time may be expected during staff shortages even when the examining laboratory is within the same medical treatment facility that collected the Pap smear.

Electronic imaging provides an opportunity for eliminating several of the delays associated with this process. Time during which cases are aggregated, slides are mailed, and reports returned may, in principle, be significantly reduced by basing case diagnosis on transmitted electronic images. In addition, delays resulting from staff shortages may be obviated, since the impact of losing one or two cytotechnologists (which may be half the staff of even a relatively large military cytocenter) is small when compared to the aggregate cytotechnologist staffing of military medical facilities. In our conceptual model of the distributed cytopathology laboratory, steps 2 to 4 of the process above are replaced with the following sequence:

2. Information for the SF541 is entered on a computer in the gynecology clinic, using a "point and click" menu system. Slides are stained using a small automated staining system, then loaded on an automated prescreening device which identifies the most abnormal fields. Images of the most abnormal fields are transmitted electronically to one or more central image databases, from which they may be retrieved for examination. This process is completed within a few hours after the specimen is obtained.

3. The case is assigned to a cytotechnologist working at any installation within the DICL network of laboratories. Prescreened images are examined. If no abnormality is identified, a final report issued; this appears within minutes in the clinic. If an abnormality is identified, abnormal fields to be examined further are identified (electronically dotted) by the cytotechnologist; the case is automatically assigned to a senior cytotechnologist or pathologist working anywhere within the distributed laboratory. Following examination, the final report is

issued and transmitted to the clinic.

As envisioned, the process reduces by 10 to 12 days the turnaround time for issuing a cytopathology report. Furthermore, it enables qualified cytopathologists working anywhere within the military medical laboratory community to conduct the review examination.

Feasibility Requirements

The following points must be established in order to establish feasibility of establishing a nationwide (worldwide) military distributed cytopathology laboratory.

1. There must be available an automated prescreening technology which enables sufficiently accurate identification of abnormal fields to permit selective screening of predetermined images by a cytotechnologist. Alternatively, technology must allow allow digitization and transmission of images representing the complete microscope slide at a resolution permitting cytologic diagnosis.

2. Images must be of sufficiently high quality to allow initial screening?

3. Abnormal fields must be identified sufficiently precisely by cytotechnologists to allow "electronic dotting" and examination by a cytopathologist.

4. Image database systems and case routine/scheduling algorithms must allow easy implementation of the DICL concept without undue waiting on the part of cytotechnologists and cytopathologists.

Feasibility Demonstration

In order to demonstrate "proof of concept", we propose to demonstrate a working prototype of the above system in a four phase process. In phase I, represented by this proposal, we will demonstrate the efficacy of "electronic dotting" by cytotechnologists, together with the accuracy of final reporting by the pathologist. This is a necessary, though not sufficient, condition for success of the DICL concept, and is the least expensively demonstrated of all feasibility requirements. Specifically, we will:

1. Implement a system for integrating electronic images with the demographic/clinical information required for cytologic examination.

2. Implement a system to allow cytotechnologists to capture

digital images of abnormal fields at the microscope.

3. Implement a system for examination of digital images and clinical data by a pathologist at a site remote from that of the cytotechnologist.

4. Determine the accuracy of final diagnoses rendered by pathologists using electronic images acquired by the cytotechnologists.

The result of this study will be a working prototype of part of the DICL system (based on a Mosaic/WWW implementation), utilizing resources at the University of Michigan and the Armed Forces Institute of Pathology. In addition, Phase I will develop the information to allow an intelligent assessment of whether the concept should be further investigated.

Assuming successful completion of Phase I, Phase II will integrate an automated prescreening system and an automated data management system, with an image database and workload scheduling system. Completion of Phase II will allow demonstration of a complete prototype system. Phase III will develop a compact, field-deployable prototype system. Phase IV will constitute of multi-institution test of the DICL concept.

RESOURCES REQUIRED (Phase I)

The project as defined above will require one year to complete, and will utilize the following resources:

Principal Investigator:	10%	no salary requested
Associate Investigator (AFIP):	10%	no salary requested
Associate Investigator (U of Michigan)	10%	$20,000
Cytotechnologist (AFIP):	10%	no salary requested
Computer programmer (U of Michigan):	25%	$15,000
Computer programmer (AFIP):	50%	30,000
Supplies and contractual costs:		10,000
Travel:		4,000
Total:		79,000

HUMAN USE

This study will depend upon existing pathological material and is classified as exempt.

INVESTIGATORS

See attached curricula vitae.